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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,672	THNONNARD, JOELLE	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,30,33,35,36,39,44,45 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30,33,35,39,44,45 and 51-54* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicant's amendment filed on 2/16/05 is acknowledged.

Status of claims

2. Claims 29, 31, 32, 34, 37, 38, 40-43, 46 and 48 - 50 are canceled.

Claims 28, 39, 45, 47 have been amended.

New claims 51-54 have been added. Newly added claims 51-54,drawn to polypeptide and therefore are included to the elected invention.

Claims 27, 35, 38, 43, 44, 46, and 51-54 are pending and are under examination.

Priority

3. Applicant states that the certified priority document U.K 9914945031.2 (priority under 35, U.S.C. 119 (a)- (d)), 6/25/1999) will be submitted in due course.

Claim Objection

4. The examiner regrets in objecting claim 47 as being an incomplete sentence in the previous office action (8/16/04). Applicant amended 2/16/05 claim 47 to recite "to a mammal" in response to examiner's objection. However, the limitation "to a mammal " in claim 47 is now admitted to be redundant as the claim 47 recites "A method for inducing an immune response in a mammal---". Accordingly, applicant may wish to amend claim 47 to original claim 47 and delete "to a mammal". The examiner regrets the inconvenience to applicants.

Specification Informalities withdrawn

5. In view of amendment to the specification, the examiner has withdrawn the specification informalities.

As stated by the applicant, recitation of XL Fit software program is well known, therefore, the specification informality is also withdrawn.

Claim Rejections - 35 USC 112, second paragraph withdrawn

6. In view of amendment to the claim, the rejection of claim 45 under 35 U.S.C. 112, second paragraph is withdrawn

Claim Rejections - 35 USC 102 withdrawn

7. In view of amendment to the claims, the rejection of claims 28, 33, 35, 39, 44, 45, 47 under 35 U.S.C. 102(e) as being anticipated by Breton U.S.Patent 6673910 is withdrawn

Claim Rejections - 35 USC 112, first paragraph maintained

8. The written description rejection of claims 28, 33, 35, 39, 44, 45, 47 and newly added claims 51-54 under 35 U.5.C. 112, first paragraph is maintained for the same reasons as set forth in the previous office action.

The specification describes as part of the invention, an isolated polypeptide comprising the amino acid sequence, SEQ ID NO: 2, which is encoded by BASB111 gene from *M.catarrhalis* strain Mc 2931, ATCC 43617. The specification also teaches that this full-length protein contains 276 amino acids and is useful in diagnosing *M.catarrhalis* infection. However, the immunological function of this gene or its product in assessing Otitis media has not yet been identified. Further, the specification does not an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids or vaccine comprising said fragments (i.e., 15 amino acids or 20 amino acids) or fusion protein comprising said fragments (i.e., 15 amino acids or 20 amino acids). Therefore, said fragments do not meet the guidelines on written description.

The specification fails to disclose any substitution, insertion or deletion or change in a polypeptide SEQ.ID.NO: 2 to obtain an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids. The specification does not describe any use of said fragments as claimed (comprising, open language) in identifying *M.catarrhalis infection* (Ottis media). None of the above fragments meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach the claimed fragments and do not satisfy the written description guidelines because an isolated immunogenic polypeptide comprising (open

language) at least 15 amino acids plus unlimited and unknown amino acids and an isolated polypeptide comprising 20 amino acids 2 plus unlimited and unknown amino acids would result in an unknown fragments without any structure and other identifying characteristics such as function. Thus, fragments as claimed are broader than SEQ.ID.NO: 2. Further, inducing an immune response is not an identifying characteristic (function) of a fragment because there are many fragments with the same function in a polypeptide and such variants are not distinguishable from each other. Thus variants as claimed are uncharacterized by this specification and are not asserted to belong to any known family of proteins such as outer membrane proteins of *M.catarrhalis*. The specification fails to teach the structure or relevant identifying characteristics sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Applicants' arguments filed on 2/16/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that the specification discloses immunogenic fragment of BASB119 polypeptide that is a contiguous portion of the polypeptide and thus applicants are in possession of the claimed invention.

The examiner understands that the specification discloses the SEQ.ID.NO: 2 and therefore, applicants are in possession of an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 2 and an isolated polypeptide consisting of an immunogenic polypeptide fragment **consisting** of 15 or 20 contiguous amino acids of SEQ.ID.NO: 2, wherein the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or suitable carrier coupled to the polypeptide, induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO: 2. However, the specification does not disclose an isolated polypeptide **comprising an** immunogenic polypeptide **comprising** a fragment of **at least** 15 or 20 contiguous amino acids of SEQ.ID.NO: 2 as claimed because the claimed polypeptides with open claim language are broader than SEQ.ID.NO: 2. Therefore, the

rejection is maintained as the specification fails to teach the claimed fragments and do not satisfy the written description guidelines because an isolated polypeptide comprising (open language) at least 15 amino acids plus unlimited and unknown amino acids would result in an unknown fragments without any structure and other identifying characteristics such as function.

9. The scope rejection of claims 28, 33, 35, 39, 44, 45, 47 and newly added claims 51-54 under 35 U.5.C. 112, first paragraph is maintained for the same reasons as set forth in the previous office action.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is drawn to recombinant isolated polypeptide comprising the amino acid sequence, SEQ ID NO: 2, which is encoded by BASB111 gene from *M.catarrhalis* strain Mc 2931, ATCC 43617. The specification also teaches that the full-length polypeptide, SEQ.ID.NO: 2 contains 276 amino acids and is useful in diagnosing *M.catarrhalis* infection. Further, the invention teaches that the polypeptide, SEQ.ID.NO: 2 could be used as an immunogen in formulating immunogenic composition in Freund's adjuvant to immunize mice for raising anti polypeptide, SEQ.ID.NO: 2 antibodies.

The state of the art prior art is devoid of making or using fragments such as an isolated immunogenic polypeptide comprising (open language) at least 15 amino acids plus unlimited and unknown amino acids and an isolated immunogenic polypeptide comprising 20 amino acids 2 plus unlimited and unknown amino acids as claimed broadly in bacterial infections especially in *M.catarrhalis* infections.

The predictability of making and using fragments of a polypeptide in generating antibodies, sufficient to specifically diagnose otitis media and respiratory disease caused by Moraxella catarrhalis infections or sufficient to elicit a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infection is acknowledged to be unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of

Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide.

The specification provides no working examples demonstrating (i.e., guidance) enablement for an immunogenic fragment comprising (open language) at least 15 amino acids or 20 amino acids plus unlimited amino acids, fusion protein comprising said fragments, immunogenic composition comprising said fragments of SEQ ID NO: 2 or a method of diagnosing *M.catarrhalis* infection using said broadly claimed fragments. Furthermore, it is unclear whether an immunogenic polypeptide comprising at least 15 amino acids or 20 amino acids, fusion protein comprising said fragments of *M.catarrhalis.* can be used for identifying *M.catarrhalis.* infection. Thus, fragments comprising at least 15 or 20 amino acids must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using fragments of SEQ.ID.NO: 2 because it fails to provide guidance how a fragment of SEQ.ID.NO: 2 is useful in diagnosing *M.catarrhalis* infections or for screening anti-microbial drugs. The specification does not teach and provide any guidance how to make an immunogenic polypeptide comprising a fragment of at least 15 or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed structure of the claimed polypeptide fragments of SEQ ID NO: 2 and their use in identifying specific *M.catarrhalis* infections. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Applicants' arguments filed on 2/16/05 have been fully considered but they are not deemed to be persuasive.

Applicants' arguments filed on 2/14/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that the instant application provides full disclosure of the amino acid sequence SEQ.ID.NO: 2 and the nucleotide sequence SEQ.ID.NO: 1, which encodes the polypeptide SEQ.ID.NO: 2 ii) substantial guidance has been provided in specification on

pages 45-47 and also one of ordinary skill in the art has ability and skill to produce fragments iii) the examiner's concerns regarding "unlimited and unknown amino acids" of SEQ.ID.NO: 2 are misplaced and the claims do not encompass unlimited and unknown amino acids" because applicant is claiming immunogenic fragments of SEQ.ID.NO:2 and claims are properly enabled. The examiner understands that the specification discloses the SEQ.ID.NO: 2 and therefore, applicants are enabled for an immunogenic fragment **consisting** of 15 contiguous amino acids of SEQ.ID.NO: 2, wherein the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or suitable carrier coupled to the polypeptide, induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO: 2. However, the specification does not disclose an immunogenic fragment **comprising at least** 15 contiguous amino acids of SEQ.ID.NO: 2 as claimed and these fragments are broader than SEQ.ID.NO: 2.

With respect to fragments of said polypeptide, the examiner understands that the specification teaches the amino acid sequence SEQ.ID.NO: 2 and therefore enabled for an isolated polypeptide consisting of an immunogenic fragment of 15 contiguous amino acids of SEQ.ID.NO: 2. However, applicant is claiming an isolated polypeptide comprising of at least 15 contiguous amino acids of SEQ.ID.NO: 2. Recitation of open language " comprising " in the claims does not limit to the fragments of SEQ.ID.NO: 2 but reads on fragments of SEQ.ID.NO: 2 plus other unknown and unlimited amino acids and are not supported by the present specification, pages 45-47.

With respect to the unpredictability of protein chemistry, applicant noted the art recognized difficulties in processing (via antigen presenting cell) the fragments for inducing a T-cell response. Further applicant states that methods were available to overcome these difficulties at the time of the filing of the instant application for example in Reece et al, Exhibit A

the difficulties of protein processing were overcome by synthesizing overlapping dodecapeptides on pins to map T-cell epitopes of tetanus toxin. Pools of peptides were used to simplify the mapping assays. Thus, it was practical to synthesize a large number of peptides, and the initial screen needed only to assay sixty to seventy pools. Pools that generated strong responses were deconvoluted by assaying the members of the pool and such multipin methods were taught in the art such as Current Protocols in Immunology, 1997 (Exhibit B) and Reece et al. 172 J. Immunol. 1994 241 (Exhibit C). Applicant states that the examiner's concerns regarding "unlimited and unknown amino acids" of SEQ.ID.NO: 2 are misplaced.

The examiner has reviewed exhibits A, B and C carefully and understands that epitope mapping using overlapping synthetic peptide pools and assaying such pools using multipin method are known in the art. Here, the issue here is whether immunogenic fragment **comprising** of at least 15 contiguous amino acids of SEQ.ID.NO: 2 as claimed is enabled or not. As discussed above, applicant is enabled only for immunogenic fragment consisting of 15 contiguous amino acids of SEQ.ID.NO: 2. The art submitted by the applicant also clearly indicates that specific small peptides are important in epitope mapping and thus supporting the examiner's position (i.e., **immunogenic fragment consisting of 15 contiguous amino acids of SEQ.ID.NO: 2**). Further, the art teaches longer the peptide, the lower will be the purity of the peptide and therefore, synthesis of peptides that are longer than 6 residues should be avoided (see Exhibit B, unit 9.7.5, third paragraph under assessing peptide sequences). Exhibit C teaches that many epitopes (see abstract) would be missed if the peptides used were long (31mer, Table 2). Thus, the art teaches the specific peptide is critical for identifying successful T-helper epitope and therefore, immunogenic fragment consisting of 15 contiguous amino acids of SEQ.ID.NO: 2 are suitable for mapping but not the polypeptide **comprising** an immunogenic

fragment of **"at least"** 15 contiguous amino acids as it reads on unknown fragments that are broader than SEQ.ID.NO: 2.

Applicant is not claiming peptides **consisting of 15 amino acids of SEQ.ID.NO: 2** but claiming an isolated polypeptide **comprising** an immunogenic fragment of **"at least"** 15 contiguous amino acids of SEQ.ID.NO: 2. The limitation "at least " in the claims does not limit to 15 contiguous amino acids because it has no upper limit and thus reads on fragments having more than 15 amino acids in length. Similarly the limitation "comprising" leaves " the claim open for the inclusion of unspecified ingredients even in major amounts and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. Therefore, the claimed immunogenic fragment is larger than amino acids (15 amino acids plus unlimited amino acids) in length. Hence examiner's concern regarding the language used is important in claiming immunogenic fragments.

Evidentiary references as discussed above clearly indicated the use of short 12 – mer peptide sequences for mapping and screening epitopes of a larger protein (i.e., fragment **consisting** of 15 contiguous amino acid sequence of SEQ.ID.NO: 2) to reveal immunodominant regions of the antigen. In addition, Molloy et al (Molecular Immunol. 35, 1998, pages 73-81) teach, production of TCR (TCR comprising two other immunoglobulin super family member proteins) epitope has remained problematic as the majority of the recombinant proteins remains insoluble and is not processed. Therefore, the claimed isolated recombinant polypeptide comprising an immunogenic fragment of at least 15 contiguous amino acids of SEQ.ID.NO: 2 (a larger immunogenic fragment) for mapping t-cell epitopes must be considered highly unpredictable requiring a specific demonstration of efficacy of the polypeptide in mapping epitopes. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

10. The rejection of claims 44-45 and claim 28 (as a vaccine composition only) under 35 U.S.C. 112, first paragraph is maintained for the same reasons as set forth in the previous office action.

Claims are drawn to a vaccine composition comprising an isolated polypeptide comprising a member selected from the group consisting of an amino acid sequence matching SEQ.ID.NO: 2 and an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids and at least one other *M.catarrhalis* antigen in a pharmaceutically acceptable carrier.

Instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The definition of "vaccine" is broad, it is not so broad to cover **any** use of a substance on or in the body of a subject, only those uses intended to prevent, treat, or cure a disease within the animal to which the substance was administered.

Enablement of a "vaccine composition" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed vaccine is for the treatment of otitis media and respiratory disease caused by Moraxella catarrhalis infections. Thus, the nature of the invention is a therapeutic composition used in the treatment or prevention. In the instant application, the animal to which the claimed composition is administered is merely being used as a bioreactor to make the antibodies (example 5) that will ultimately be used *in vitro*. In addition, the instant specification does not teach how to use the composition, without undue experimentation, for the prevention, treatment, or cure of a disease in the animal to which the substance is administered.

The specification discloses the claimed composition as a vaccine can be used in mice model (example 3). There is insufficient guidance which would enable one skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infections. At the time the invention was made, vaccines comprising the claimed polypeptide/fragments were not routinely used for the treatment of otitis media and respiratory diseases. The specification lacks guidance by way of general methods or working examples which teach an "effective amount" of the vaccine which would be used for this purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of otitis media and respiratory diseases. It is unpredictable whether the claimed composition, which is disclosed as being only immunogenic, would have the added property of generating the protective immune response sufficient to inhibit the otitis media and respiratory diseases because the prior art discloses that vaccine development is at the antigen identification stage and testing of these protective antigens is by testing them in animal models or clinical testing of these antigens (see review article by McMichael, 2000, Microbes and Infection 2; 561-568) The specification has not disclosed a link or nexus between

generating protective immunity using the claimed polypeptide/fragments and preventing or curing *M.catarrhalis* infections or Ottis media. Further, it is not common in the art of immunotherapy to use the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

It is acknowledged that weight is given to every term in claims 44-45. This is why the instant claims drawn to vaccines are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same composition and formulations thereof as claimed.

Applicants' arguments filed on 2/16/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that the specification provides ample teachings (pages 37-42) that one skilled would understand as fully enabling and recognize that the experimentation required to make the invention of claims 44 and 45 is within the normal experimentation in this are of making vaccines. This is fully supported by the McMichael article supplied by the examiner.

The examiner disagrees with the applicant because the examiner reviewed the specification pages 37-42 and found the general description of inducing cytokines that tend to favor the induction of cell mediated immune responses and humoral immune responses to the antigen. However, applicant's specification does not disclose and there is no evidence of record that the claimed polypeptide/fragments would generate an immune response such that one could use it for the treatment of otitis media or respiratory diseases. Further, as indicated above the claimed **uncharacterized antigens** have not been shown to induce an immune response that could prevent the infection as the claimed invention is drawn to a vaccine composition. The reference supplied by the examiner clearly sets forth that a single antigen may prove insignificant and a mixture of antigens capable of eliciting antibodies with more than one functional capacity may be needed. Further, the art states that in addition to candidate vaccine

identification, other vaccine issues need to be answered for example, optimal mode of vaccine delivery such as parenterally delivered vaccine. Based on the general (issues) problems regarding the identification of candidate vaccine, the experimentation required to use the claimed uncharacterized antigens is "undue".

Claim Rejections - 35 USC 102 maintained

11. The rejection of claims 28, 30, 33, 35, 44, 45 and newly added claims 51-54 under 35 U.S.C. 102(b) as being anticipated by Christensen et al Clin Diagn Lab Immunol. 1996 Nov; 3(6): 717-21 is maintained for the same reasons as set forth in the previous office action.

Christensen et al disclose isolated polypeptides by SDS-PAGE from outer membrane proteins i.e., OMP from different strains, in a buffer (pharmaceutical carrier) from M.catarrhalis (see materials and methods).

The OMP patterns obtained by SDS-PAGE of the seven *M. catarrhalis* strains were shown in Fig. 1. Approximately 25 bands with molecular masses of between 140 and 16 kDa could be identified, with six to eight of these being the major bands A to H, with molecular masses of 98, 84, 72, 69, 56, 43, 28, and 21 kDa recognized for individual strains.

The lower-molecular-weight OMP 28 kD (figure 1, see in the next page) polypeptide appears to be same as the claimed polypeptide, SEQ.ID.NO: 2 having 276 amino acids because molecular weight of an amino acid is approximately 110 daltons. Therefore, 28 kD protein read on claims. The disclosed OMP preparations read on immunogenic composition as outer membrane proteins bind to the convalescent sera (see figure2). Thus, the prior art anticipated claims 28, 30, 33 and 35. The same OMP preparation reads on a vaccine composition because vaccine is treated as intended use of said composition recited in claims 44 and 45. As OMP contains several antigens in the preparation, it meets the limitation "one other Moraxella antigen" of claim 45.

Outer membrane 28kD protein from M.catarrhalis inherently contains an isolated polypeptide comprising SEQ.ID.NO: 2 as it contains all proteins produced by this organism. Characteristics such as SEQ.ID.NO: 2 are considered as inherent properties of the 28kD polypeptide that was present in the OMP disclosed by the prior art. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 2 with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 2/16/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that claims do not read on the prior art because Christensen does not disclose **the** amino acid sequence and discloses whole cell lysates.

The examiner disagrees with the applicant because the claim 28 does not recite an isolated polypeptide comprising **the** amino acid sequence SEQ.ID.NO: 2. Recitation of "an amino acid" and a "fragment" in the claims read on polypeptide comprising with two amino acids. The OMP preparations of the prior art read on the claimed invention as discussed above. Claims 51-52 are also rejected under this rejection because recitation of "recombinant" in the claim 51 is viewed as a process limitation because the prior art OMP and the claimed polypeptide appear to be the same.

12. The rejection of claims 28, 33, 35 and newly added claims 51-54 under 35 U.S.C. 102(b) as being anticipated by Murphy et al 1993, Database: PIR_78, Acession number JN0751 is maintained for the same reasons as set forth in the previous office action

Murphy et al in Acession number JN0751disclose an isolated polypeptide comprising an immunogenic polypeptide comprising a fragment of at least 15 amino acids or 20 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO: 2 (please see the sequence alignment, 3rd line from position 140-173, QY represents SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein) and thus anticipated claims 28, 33, 35 and 51, 53, and 54. The prior art polypeptide reads on claims because the disclosed immunogenic fragment comprises more than 20 amino acids and is common in the art of immunology to use a peptide with five amino acids to induce an antibody response in animals, therefore, the disclosed polypeptide comprising 276 amino acids is inherently immunogenic and thus comprises an immunogenic fragments as claimed in claims. Therefore, the claimed invention is anticipated by the prior art.

Applicants' arguments filed on 2/16/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that claims have been amended and therefore, the prior art does not read on the amended claims.

The examiner disagrees with the applicant because the amended claim 28 (b) is drawn to an immunogenic polypeptide comprising a fragment sequence of 15 or 20 contiguous amino acids from **1-46 or 104-276** of SEQ.ID.NO: 2 and rightly Murphy et al disclosed an isolated polypeptide or an immunogenic polypeptide comprising a fragment of at least 15 amino acids or 20 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO: 2 (please see the sequence alignment, 3rd line from position 140-173, QY represents SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein). Thus, Murphy et al Acession number JN0751 anticipated the claims 28, 33, 35, 51, 53, and 54.

Remarks

13. No claims are allowed

Applicant did not respond to examiner's reference to brief description of the drawing(s) made in the previous office action.

Conclusion

14 Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

1. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D

L. R. S.
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600